UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/622,076	07/17/2003	Rudolf Gilmanshin	C0989.70054US00	1842

7590 03/06/2007

Helen C. Lockhart
Wolf, Greenfield & Sacks, P.C.
Federal Reserve Plaza
600 Atlantic Avenue
Boston, MA 02210

EXAMINER	
BERTAGNA, ANGELA MARIE	
ART UNIT	PAPER NUMBER
1637	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/06/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No. 10/622,076	Applicant(s) GILMANSHIN, RUDOLF	
	Examiner Angela Bertagna	Art Unit 1637	

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 December 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,5-9,11-17,19-34,68,91 and 125-130* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,5-9,11-17,19-34,68,91 and 125-130* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/3/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

FINAL REJECTION

Status of the Application

1. Applicant's response filed December 4, 2006 is acknowledged. Claims 1, 2, 8, 9, 11, 12, 14, 15, 22, 23, 31-34, 68, 91, and 125-127 were amended, and claims 3, 4, 10, 18, 35-67, and 69-90, and 92-124 were cancelled.

Information Disclosure Statement

2. The Information Disclosure Statement filed August 3, 2006 has been considered. A signed copy is enclosed herewith.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 5-9, 11-17, 19-34, 68, 91, and 125-130 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 2, 5-9, 11-17, and 19-34 are indefinite, because independent claim 1 recites the limitation "the polymer" in lines 2, 4, 6, 7, and 8. There is insufficient antecedent basis for this limitation in the claim.

Claim 68 recites the limitation "the polymer" in lines 3-5, 7, 8, and 10. There is insufficient antecedent basis for this limitation in the claim.

Claim 91 recites the limitation "the polymer" in line 8. There is insufficient antecedent basis for this limitation in the claim.

Claims 125-128 are indefinite, because independent claim 125 recites the limitation "the polymer" in lines 2, 4, and 5. There is insufficient antecedent basis for this limitation in the claim.

Claims 129 and 130 recite the limitation "the polymer" in lines 2 and 4-6 (claim 129) and lines 2, 4-6, and 8 (claim 130). There is insufficient antecedent basis for this limitation in the claims.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1, 2, 5, 6, 11, 13-15, 21-27, 31, 32, 91, and 125-130 are rejected under 35 U.S.C. 102(b) as being anticipated by Kigawa et al. (US 5,965,361; newly cited).

Regarding claim 1, Kigawa teaches a method for analyzing a nucleic acid polymer (see Example 3, columns 16-17) comprising:

(a) contacting the polymer with a conjugate comprising a nucleic acid tag molecule and a nucleic acid binding enzyme (column 17, lines 5-25, where a conjugate comprising a biotinylated nucleic acid molecule (the "nucleic acid tag molecule") and Cy3-labeled RecA (the

nucleic acid binding enzyme) is added to a target nucleic acid; column 16, lines 5-45 teach preparation of the nucleic acid probe/Rec A conjugate; alternatively, see column 4, lines 7-25)

(b) allowing the nucleic acid binding enzyme to bind the polymer nonspecifically (column 17, lines 5-25; see also column 2, lines 39-44)

(c) allowing the nucleic acid tag molecule to bind specifically to the polymer (column 17, lines 5-25; see also column 4, lines 16-18 and column 6, lines 11-15)

(d) determining a pattern of binding of the conjugate to the polymer (column 17, lines 59-67; see also column 4, lines 27-31)

wherein the nucleic acid binding enzyme binds to the polymer without cleavage (Kigawa does not teach cleavage of the polymer in response to RecA binding) and is not detected based on its catalytic activity (see column 17, lines 59-67, where detection is based fluorescence of a Cy3 label attached to RecA or a signal of FITC derived from the biotinylated probe).

Regarding claim 2, in the method of Kigawa the RecA protein translocates along the polymer (column 2, lines 39-44).

Regarding claim 5, Kigawa teaches that the polymer is DNA (column 4, lines 47-49).

Regarding claim 6, Kigawa teaches that the nucleic acid tag molecule is a DNA (column 5, lines 57-59).

Regarding claim 11, Kigawa teaches that the enzyme is a DNA repair enzyme (see abstract, where RecA is taught).

Regarding claims 13-15 and 27, Kigawa teaches that the nucleic acid tag molecule is labeled with a first detectable moiety (or agent) and the nucleic acid binding enzyme is labeled with a second detectable moiety (see Example 3, column 17, lines 59-67, where Kigawa teaches

that RecA is labeled with the Cy3 fluorophore and the nucleic acid tag molecule is labeled with biotin; see also column 6, lines 22-32, where Kigawa teaches labeling of the nucleic acid tag and RecA).

Regarding claim 21, Kigawa teaches detection using FISH (see Example 3, column 17, lines 59-67).

Regarding claims 22 and 23, Kigawa teaches that the detectable moiety is a fluorescent molecule and that detection proceeds using a fluorescence detection system (column 6, lines 22-25; see also column 17, lines 59-67, where FITC fluorescence derived from the biotinylated nucleic acid tag molecule is detected using a fluorescence microscope).

Regarding claims 24-26, Kigawa teaches examples of nucleic acid tag molecules that are not in vitro amplified nucleic acids (see column 16, lines 5-18; see also column 5, line 57 – column 6, line 10). Kigawa also does not teach that the nucleic acid tag molecules are antisense molecules. Finally, the probe taught by Kigawa in Example 3 is specific for a human chromosome 1 satellite III sequence (column 16, lines 5-7). This is not a bacterial or viral-specific sequence.

Regarding claims 31 and 32, Kigawa teaches that the nucleic acid binding enzyme is detected indirectly, specifically by binding of an antibody specific to the enzyme (column 3, line 64 – column 4, line 5).

Regarding claim 91, Kigawa teaches a method for analyzing a nucleic acid molecule comprising:

(a) exposing a nucleic acid molecule to a conjugate of a nucleic acid tag molecule and a nucleic acid binding enzyme (column 17, lines 5-25, where a conjugate comprising a

biotinylated nucleic acid molecule (the "nucleic acid tag molecule") and Cy3-labeled RecA (the nucleic acid binding enzyme) is added to a target nucleic acid; column 16, lines 5-45 teach preparation of the nucleic acid probe/Rec A conjugate; alternatively, see column 4, lines 7-25)

(b) allowing the nucleic acid binding enzyme to bind the nucleic acid molecule (column 17, lines 5-25; see also column 2, lines 39-44)

(c) allowing the nucleic acid tag molecule to bind to the nucleic acid molecule in a sequence-specific manner (column 17, lines 5-25; see also column 4, lines 16-18 and column 6, lines 11-15)

(d) determining a pattern of binding of the conjugate to the polymer (column 17, lines 59-67; see also column 4, lines 27-31)

wherein the nucleic acid binding enzyme binds to the polymer without cleavage (Kigawa does not teach cleavage of the polymer in response to RecA binding) and is not detected based on its catalytic activity (see column 17, lines 59-67, where detection is based fluorescence of a Cy3 label attached to RecA or a signal of FITC derived from the biotinylated probe).

Regarding claim 125, Kigawa teaches a method for analyzing a nucleic acid polymer comprising:

(a) contacting the polymer with a conjugate comprising a nucleic acid tag molecule and a nucleic acid binding agent (column 17, lines 5-25, where a conjugate comprising a biotinylated nucleic acid molecule (the "nucleic acid tag molecule") and Cy3-labeled RecA (a nucleic acid binding agent) is added to a target nucleic acid; column 16, lines 5-45 teach preparation of the nucleic acid probe/Rec A conjugate; alternatively, see column 4, lines 7-25)

(b) allowing the nucleic acid binding agent to bind the polymer (column 17, lines 5-25; see also column 2, lines 39-44)

(c) allowing the nucleic acid tag molecule to bind to specifically bind the polymer (column 17, lines 5-25; see also column 4, lines 16-18 and column 6, lines 11-15)

wherein the nucleic acid binding agent is a DNA repair enzyme (column 16, lines 5-45 and column 4, lines 7-25 teach that the binding agent is the DNA repair enzyme RecA).

Regarding claims 126-128, Kigawa teaches a method for labeling a nucleic acid polymer comprising:

(a) contacting the polymer with a conjugate comprising a nucleic acid tag molecule and a nucleic acid binding enzyme (column 17, lines 5-25, where a conjugate comprising a biotinylated nucleic acid molecule (the "nucleic acid tag molecule") and Cy3-labeled RecA (a nucleic acid binding enzyme) is added to a target nucleic acid; column 16, lines 5-45 teach preparation of the nucleic acid probe/Rec A conjugate; alternatively, see column 4, lines 7-25)

(b) allowing the nucleic acid binding enzyme to bind non-specifically and translocate along the polymer (column 17, lines 5-25; see also column 2, lines 39-44)

(c) allowing the nucleic acid tag molecule to bind specifically to the polymer thereby labeling the polymer (column 17, lines 5-25; see also column 4, lines 16-18 and column 6, lines 11-15)

(d) determining a pattern of binding of the conjugate to the polymer (column 17, lines 59-67; see also column 4, lines 27-31)

wherein the nucleic acid binding enzyme binds to the polymer without cleavage (Kigawa does not teach cleavage of the polymer in response to RecA binding) and is not detected based

on its catalytic activity (see column 17, lines 59-67, where detection is based fluorescence of a Cy3 label attached to RecA or a signal of FITC derived from the biotinylated probe).

Regarding claim 129, Kigawa teaches a method for analyzing a nucleic acid polymer comprising:

(a) contacting the polymer with a conjugate comprising a nucleic acid tag molecule and a nucleic acid binding enzyme (column 17, lines 5-25, where a conjugate comprising a biotinylated nucleic acid molecule (the "nucleic acid tag molecule") and Cy3-labeled RecA (a nucleic acid binding enzyme) is added to a target nucleic acid; column 16, lines 5-45 teach preparation of the nucleic acid probe/Rec A conjugate; alternatively, see column 4, lines 7-25)

(b) allowing the nucleic acid binding enzyme to bind to the polymer (column 17, lines 5-25; see also column 2, lines 39-44)

(c) allowing the nucleic acid tag molecule to bind specifically to the polymer (column 17, lines 5-25; see also column 4, lines 16-18 and column 6, lines 11-15)

(d) determining a pattern of binding of the conjugate to the polymer (column 17, lines 59-67; see also column 4, lines 27-31)

wherein the nucleic acid binding enzyme is a nuclease that binds to the polymer without cleavage (Kigawa does not teach cleavage of the polymer in response to RecA binding) and is not detected based on its catalytic activity (see column 17, lines 59-67, where detection is based fluorescence of a Cy3 label attached to RecA or a signal of FITC derived from the biotinylated probe).

Regarding claim 130, Kigawa teaches a method for analyzing a nucleic acid polymer comprising:

(a) contacting the polymer with a conjugate comprising a nucleic acid tag molecule and a nucleic acid binding enzyme (column 17, lines 5-25, where a conjugate comprising a biotinylated nucleic acid molecule (the “nucleic acid tag molecule”) and Cy3-labeled RecA (a nucleic acid binding enzyme) is added to a target nucleic acid; column 16, lines 5-45 teach preparation of the nucleic acid probe/Rec A conjugate; alternatively, see column 4, lines 7-25)

(b) allowing the nucleic acid binding enzyme to bind non-specifically (column 17, lines 5-25; see also column 2, lines 39-44)

(c) allowing the nucleic acid tag molecule to bind specifically to the polymer (column 17, lines 5-25; see also column 4, lines 16-18 and column 6, lines 11-15)

(d) determining a pattern of binding of the conjugate to the polymer based on detection of the nucleic acid tag molecule and not the nucleic acid binding enzyme (column 17, lines 59-67, where the FITC signal derived from the biotinylated probe is detected)

wherein the nucleic acid binding enzyme binds to the polymer without cleavage (Kigawa does not teach cleavage of the polymer in response to RecA binding).

6. Claims 1, 2, 5-9, 11-13, 16, 17, 22-25, 27-31, 91, and 126-130 are rejected under 35 U.S.C. 102(b) as being anticipated by Ecker et al. (US 5,986,053; cited on IDS filed August 3, 2006).

Regarding claim 1, Ecker teaches a method for analyzing a nucleic acid polymer (see Examples 27-28, columns 30-31) comprising:

(a) contacting the polymer with a conjugate comprising a nucleic acid tag molecule and a nucleic acid binding enzyme (column 31, lines 1-7, where a DNA fragment is contacted with a PNA (nucleic acid tag molecule) and RNA polymerase)

(b) allowing the nucleic acid binding enzyme to bind the polymer nonspecifically (column 31, lines 1-7)

(c) allowing the nucleic acid tag molecule to bind specifically to the polymer (column 31, lines 3-4 teach that the PNA-DNA complexes are formed as in Example 26, which in turn references Example 25. Example 25 teaches that the PNA probes are complementary to the target DNA fragment (column 30, lines 18-20)

(d) determining a pattern of binding of the conjugate to the polymer (column 31, lines 7-15, where footprinting is conducted)

wherein the nucleic acid binding enzyme binds to the polymer without cleavage (Ecker does not teach cleavage of the polymer in response to RNA polymerase binding) and is not detected based on its catalytic activity (column 31, lines 7-15 teach footprinting analysis which is not based on the catalytic activity of RNA polymerase).

Regarding claim 2, the RNA polymerase taught by Ecker inherently translocates along the polymer.

Regarding claim 5, Ecker teaches that the polymer is DNA (column 31, line 1).

Regarding claim 6, Ecker teaches that the nucleic acid tag molecule is a PNA (column 31, lines 1-4).

Regarding claim 7, Ecker teaches that the nucleic acid tag molecule is 11 residues in length (see SEQ ID NO: 1 in the Sequence Listing).

Regarding claims 8 and 9, Ecker teaches that the nucleic acid tag molecule and nucleic acid binding enzyme are covalently bound (column 12, lines 9-17) or bound to each other via a linker (column 11, lines 17-30).

Regarding claim 11, Ecker teaches that the enzyme is an RNA polymerase enzyme (see column 31, lines 4-5).

Regarding claim 12, Ecker teaches that the enzyme cannot modify the nucleic acid molecule or polymer (see Example 29, where Ecker teaches that RNA polymerase is not capable of transcription in the presence of the PNA/DNA complex).

Regarding claim 13, 22, 23, and 27, Ecker teaches that the nucleic acid tag molecule is labeled with a detectable moiety (or agent), specifically a fluorescent molecule (column 12, lines 9-12). Detection of these molecules inherently requires a fluorescence detection system.

Regarding claim 16, Ecker teaches that the polymer is labeled with a detectable moiety (column 31, lines 1-3, where the polymer is radiolabeled).

Regarding claim 17, Ecker teaches detection of the polymer using a backbone specific label (see Example 7, column 20, lines 56-67).

Regarding claims 24 and 25, Ecker teaches examples of nucleic acid tag molecules that are not in vitro amplified nucleic acids (see Example 25, column 30, lines 29-34, where the DNA

fragments used in Example 27 are not in vitro amplified molecules). Ecker also teaches that the nucleic acid tag molecules are not antisense molecules (column 12, lines 38-40).

Regarding claims 28-30, Ecker teaches that the PNA (nucleic acid tag molecule) is labeled with an agent capable of cleaving a nucleic acid molecule (column 12, lines 9-11, where nuclease conjugation is taught). This enzyme-PNA conjugate is inherently capable of modifying a nucleic acid molecule. Ecker also teaches labeling with a photocleaving agent (column 3, lines 19-20). Such agents inherently modify the nucleic acid molecule.

Regarding claim 31, Ecker teaches that the nucleic acid binding enzyme is detected indirectly (column 31, lines 7-15, where detection is based on radiolabeled nucleic acids).

Regarding claim 91, Ecker teaches a method for analyzing a nucleic acid molecule comprising:

(a) exposing a nucleic acid molecule to a conjugate of a nucleic acid tag molecule and a nucleic acid binding enzyme (column 31, lines 1-7, where a DNA fragment is contacted with a PNA (nucleic acid tag molecule) and RNA polymerase)

(b) allowing the nucleic acid binding enzyme to bind the nucleic acid molecule (column 31, lines 1-7)

(c) allowing the nucleic acid tag molecule to bind to the nucleic acid molecule in a sequence-specific manner (column 31, lines 3-4 teach that the PNA-DNA complexes are formed as in Example 26, which in turn references Example 25. Example 25 teaches that the PNA probes are complementary to the target DNA fragment (column 30, lines 18-20)

(d) determining a pattern of binding of the conjugate to the polymer (column 31, lines 7-15, where footprinting is conducted)

wherein the nucleic acid binding enzyme binds to the polymer without cleavage (Ecker does not teach cleavage of the polymer in response to RNA polymerase binding) and is not detected based on its catalytic activity (column 31, lines 7-15 teach footprinting analysis which is not based on the catalytic activity of RNA polymerase).

Regarding claims 126-128, Ecker teaches a method for labeling a nucleic acid polymer comprising:

(a) contacting the polymer with a conjugate comprising a nucleic acid tag molecule and a nucleic acid binding enzyme (column 31, lines 1-7, where a DNA fragment is contacted with a PNA (nucleic acid tag molecule) and RNA polymerase)

(b) allowing the nucleic acid binding enzyme to bind non-specifically and translocate along the polymer (column 31, lines 1-7)

(c) allowing the nucleic acid tag molecule to bind specifically to the polymer thereby labeling the polymer (column 31, lines 3-4 teach that the PNA-DNA complexes are formed as in Example 26, which in turn references Example 25. Example 25 teaches that the PNA probes are complementary to the target DNA fragment (column 30, lines 18-20)

(d) determining a pattern of binding of the conjugate to the polymer (column 31, lines 7-15, where footprinting is conducted)

wherein the nucleic acid binding enzyme binds to the polymer without cleavage (Ecker does not teach cleavage of the polymer in response to RNA polymerase binding) and is not detected based on its catalytic activity (column 31, lines 7-15 teach footprinting analysis which is not based on the catalytic activity of RNA polymerase).

Regarding claim 129, Ecker teaches a method for analyzing a nucleic acid polymer comprising:

(a) contacting the polymer with a conjugate comprising a nucleic acid tag molecule and a nucleic acid binding enzyme (column 31, lines 1-7, where a DNA fragment is contacted with a PNA (nucleic acid tag molecule) and RNA polymerase)

(b) allowing the nucleic acid binding enzyme to bind to the polymer (column 31, lines 1-7)

(c) allowing the nucleic acid tag molecule to bind specifically to the polymer (column 31, lines 3-4 teach that the PNA-DNA complexes are formed as in Example 26, which in turn references Example 25. Example 25 teaches that the PNA probes are complementary to the target DNA fragment (column 30, lines 18-20)

(d) determining a pattern of binding of the conjugate to the polymer (column 31, lines 7-15, where footprinting is conducted)

wherein the nucleic acid binding enzyme is a nuclease that binds to the polymer without cleavage (RNA polymerase inherently possesses nuclease activity, but Ecker does not teach cleavage of the fragments based on RNA polymerase activity) and is not detected based on its catalytic activity (column 31, lines 7-15 teach footprinting analysis which is not based on the catalytic activity of RNA polymerase).

Regarding claim 130, Ecker teaches a method for analyzing a nucleic acid polymer comprising:

(a) contacting the polymer with a conjugate comprising a nucleic acid tag molecule and a nucleic acid binding enzyme (column 31, lines 1-7, where a DNA fragment is contacted with a PNA (nucleic acid tag molecule) and RNA polymerase)

(b) allowing the nucleic acid binding enzyme to bind non-specifically (column 31, lines 1-7)

(c) allowing the nucleic acid tag molecule to bind specifically to the polymer (column 31, lines 3-4 teach that the PNA-DNA complexes are formed as in Example 26, which in turn references Example 25. Example 25 teaches that the PNA probes are complementary to the target DNA fragment (column 30, lines 18-20)

(d) determining a pattern of binding of the conjugate to the polymer based on detection of the nucleic acid tag molecule and not the nucleic acid binding enzyme (column 31, lines 7-15, where footprinting is conducted based on detection of the polymer; Ecker also teaches labeling the PNA with detectable labels – see column 12, lines 9-14)

wherein the nucleic acid binding enzyme binds to the polymer without cleavage (Ecker does not teach cleavage as a result of RNA polymerase binding).

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 19, 20, 33, 34, and 68 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kigawa et al. (US 5,965,361; newly cited) in view of Tegenfeldt et al. (WO 00/09757; cited previously).

Kigawa teaches the method of claim 1, as discussed above.

Regarding claims 19, 20, 33, 34, and 68, Kigawa does not teach detection using a single molecule linear polymer analysis system.

Tegenfeldt teaches a linear polymer analysis system for optically analyzing polymers (see abstract).

Regarding claim 19, the system is a linear polymer analysis system (abstract).

Regarding claim 20, Tegenfeldt teaches that the system is useful for performing a sequencing application wherein a nucleic acid is labeled with a fluorescent or radioactive label and subsequently exposed to an interaction station where the fluorescent/radioactive signal is detected (see pages 7-8, in particular the 1st full paragraph of page 8; see also claim 1).

Regarding claim 33, the system is capable of analyzing single polymers (page 8).

Regarding claim 34, the system described by Tegenfeldt is an optical mapping system (page 7, line 33 – page 8, line 4).

Regarding claim 68, Tegenfeldt teaches a method (see page 9, lines 6-15) comprising:

(a) generating optical radiation of a known wavelength to produce a localized radiation spot

(b) passing a polymer through a microchannel

(c) irradiating the polymer at the localized spot

(d) sequentially detecting radiation resulting from interaction of the polymer with the optical radiation at the localized radiation spot

(e) analyzing the polymer based on the detected radiation.

Tegenfeldt teaches the above method for the specific application of sequencing a nucleic acid molecule and also expression mapping, stating, "Since generation of expression maps involve the sequencing and identification of cDNA or mRNA, more rapid sequencing necessarily means more rapid generation of multiple expression maps (page 2, lines 3-5)."

Tegenfeldt also states, "The methods disclosed herein provide much longer read lengths than achieved by the prior art and a million-fold faster sequence reading (page 11, lines 13-14)."

It would have been prima facie obvious for one of ordinary skill in the art at the time of invention to use the detection system of Tegenfeldt to analyze the hybridization patterns produced by the method of Kigawa. Tegenfeldt expressly taught that the disclosed linear analysis system possessed several advantages compared to conventional detection methods, namely increased assay speed and the ability to analyze longer nucleic acid fragments (see page 2, lines 3-5 and page 11, lines 13-14). Since the method of Kigawa was designed for mapping applications (column 1, lines 28-32), an ordinary practitioner would have been motivated by these teachings of Tegenfeldt to substitute single molecule linear polymer analysis for FISH in order to increase the speed and efficiency of the detection step. An ordinary practitioner would have also been motivated to utilize the linear polymer analysis method of Tegenfeldt, because its single molecule detection capability (see page 8) would have increased the sensitivity of the Kigawa method. Since Tegenfeldt taught that the proposed read length is on the order of several hundred thousand nucleotides (see page 11), an ordinary artisan would have expected a

reasonable level of success in analyzing the hybridization patterns generated by the method of Kigawa using single molecule linear polymer analysis as taught by Tegenfeldt. Thus, an ordinary practitioner of the hybridization method taught by Kigawa, interested in improving the detection speed and sensitivity, would have been motivated to substitute single molecule linear polymer analysis as taught by Tegenfeldt for fluorescence in situ hybridization, thus resulting in the instantly claimed methods.

Response to Arguments

8. Claim Objections

Applicant's arguments, see page 9, filed December 4, 2006, with respect to the objection to claim 3 have been fully considered and are persuasive. Claim 3 has been canceled, and therefore the objection has been withdrawn.

Rejections under 35 U.S.C. 112, 2nd paragraph

Applicant's arguments, see pages 9-10, filed December 4, 2006, with respect to rejection of claims 33, 34, and 126-128 have been fully considered and are persuasive. Applicant's amendments overcome the rejections, and therefore they have been withdrawn.

Rejections under 35 U.S.C. 102

Applicant's arguments, see pages 10-13, filed December 4, 2006, with respect to: (a) the rejection of claims 1-8, 10, 11, 16-18, 24, 25, 27, 28, 30, 31, 91, and 125-128 as anticipated by Norton, (b) the rejection of claims 1, 3-9, 13, 14, 16, 17, 22, 24, 26, 27, 30, and 31 as anticipated

by Grigoriev, (c) the rejection of claims 1, 3-9, 16-18, 24, and 26-31 as anticipated by Magda, (d) the rejection of claims 1-11, 13-15, 18, 21-27, 30-32, 91, and 126-128 as anticipated by Hyldig-Nielsen, and (e) the rejection of claims 1-8, 10-12, 18, 24-28, 30, 31, 91, and 125-128 as anticipated by Fisher have been fully considered and are persuasive. None of these references teach all of the elements of the amended claims 1, 68, 91, 125, or 126, and therefore the rejections have been withdrawn.

Rejections under 35 U.S.C. 103

Applicant's arguments with respect to claims 19, 20, 33, 34, and 68 have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

No claims are currently allowable.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Zarling et al. (US 5,719,023) teaches analysis of a nucleic acid polymer by in situ hybridization of a RecA-oligonucleotide conjugate (see abstract).

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Angela Bertagna whose telephone number is 571-272-8291. The examiner can normally be reached on M-F, 7:30 - 5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Angela Bertagna
Examiner, Art Unit 1637
March 1, 2007

amb

JEFFREY FREDMAN
PRIMARY EXAMINER
3/2/07